COMPARISON OF
CAUDAL NEOSTIGMINE WITH BUPIVACAINE
AND CAUDAL BUPIVACAINE FOR
PAEDIATRIC POST OPERATIVE ANALGESIA

A STUDY OF 50 CASES

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE
BRANCH – X (ANAESTHESIOLOGY)

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CHENNAI, TAMILNADU

BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"Comparison of caudal neostigmine with bupivacaine and caudal bupivacaine for paediatric postoperative analgesia"** is bonafide record work done by **Dr. R. SUBHA** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfillment of University regulation for DM, Branch X –Anaesthesiology.

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DECLARATION

I **Dr.R. SUBHA** solemnly declare that the dissertation titled **"Comparison of caudal neostigmine with bupivacaine and caudal bupivacaine for paediatric postoperative analgesia"** has been prepared by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of M.D degree Branch – X (ANAESTHESIOLOGY) to be held in March 2008.

Place : Madurai **Dr. R. SUBHA**

Date :

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CONTENTS

INTRODUCTION

Pain is perhaps the most feared symptom of disease and man has tried his level best to discover methods to relieve pain. Children are special in this regard because in them it is a very complex phenomenon. The mystery is that they can feel different types of pain from same type of tissue damage, they can experience pain without injury or apparent injury

Pain has been defined by the International Association for Study of Pain[12]"as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage"

Pain relief is even more important in children who rely completely on their parents or care givers for their well being. In addition children lack communicative ability.

"For all happiness that Mankind can gain

It is not in pleasure but in relief from pain"

- John Dyrden

“Pain is an emergency for the person who experiences it regardless of the urgency of the underlying pathology, I believe we must apply the science and art of pain relief as though a life dependent upon it.”

JudithSpross(1680)

The Anaesthesiologist who does the profession of alleviating the surgical pain extends his service into the post operative period also.

A pain free post operative period is essential for both physical & psychological well being of the patient.

The physical aspects being early ambulation and early return to work.

The psychological aspects being emotional well being and confidence in the Anaesthesiologist.

Therefore in recent years more importance is given to paediatric pain relief and our duty also widens. Anaesthesiologist has to

- Choose safest technique for the children
- Provide comfort to surgeons in the intra operative period
- Good analgesia to the child in post operative period

Regional Anaesthetic technique are world wide accepted as safe and with less side effects. Among the available regional techniques caudal epidural post operative analgesia are popular in paediatrics[9].

In the advent of new drugs in epidural analgesia each drug is replacing the other because of their quality of pain relief and less side effects.

Justification :Neostigmine was chosen for this study

Neostigmine an anticholinesterase was routinely used as an reversal agent was recently shown to have effective analgesic action via caudal route with the advantage of safe, prolonged cost effective analgesia with minimal side effects(Eisenach et al 1997).

AIM OF THE STUDY

To evaluate the quality, duration and side effects of post operative analgesia with caudal neostigmine as an adjuvant with bupivacaine for paediatric caudal analgesia coming up for below umbilical surgery in the age group of 3-10 years

HISTORY

1901 - "Regional analgesia" was coined by Harvey Cushing
SICARD & CATHELIN described epidural injection through sacral hiatus.

1920 - Zwelfel was able to analyse 4200 caudal epidural injections recorded in literature.

1933 - Cambel M.F. first described sacral epidural block in children and infants.

1957 - Another milestone was synthesis of bupivacaine by Ekenstain et al

1963 - L.J. Tulivuo first used Bupivacaine clinically[26]

1974 - Kay B used caudal block for post operative pain relief in children.[15]

Jean enthuse sicard (1872-1929) and Fernard cathelin (1873-1945) independently introduced cocaine through the sacral hiatus in 1901. Sicard – Neurologist – used for treating sciatica / tabes. Cathelin – used for surgical anaesthesia, Arthur Lawen(1876-1958) a pupil of Heinrich Braun used procaine in caudal [8].

ANATOMICAL CONSIDERATIONS

Anatomy of Sacrum :

Sacrum is a large triangular bone formed by the fusion of five sacral vertebrae articulating above with 5th lumbar and below with the coccyx(8).

The base above has median / lateral positions. The median part represents the body of the 1st sacral vertebra and lateral portions, known as the alae represent fused costal and transverse elements.

The anterior surface is concave and ridged at the sites of fusion between the five sacral vertebrae. Lateral to the anterior sacral foramen through which the primary rami of the first four sacral nerve pass(8).

The posterior surface is convex and in the midline runs a bony ridge, the median sacral crest with three or four rudimentary spinous processes(8).

The lamina of 5th and sometimes the 4th sacral vertebra fails to fuse in the midline. The deficiency thus formed is known as "SACRAL HIATUS". The lateral margins of this space each bear a

prominence. “SACRAL CORNUA” – which represents the inferior articular processes of 5th sacral vertebra[8].

Sacral Canal :

It is a prismatic cavity running through out the length of the bone and following its curves. Superiorly it is triangular in its section and is continuous with lumbar epidural space.

It’s lower extremity is the sacral hiatus closed by posterior sacrococcygeal membrane which is a continuation of ligamentum flavum. Fibrous bands may be present in the canal and divide the epidural space into loculii which prevent the spread of solution and these may account for occasional incomplete anaesthesia[8].

Contents of Sacral Canal [8]:

1. The dural sac extends and ends at the lower end of 2nd sacral vertebra on a line joining the posterior superior iliac spine from the age of 2 years, compared to S3 – S4 at birth.
2. Sacral / coccygeal nerve roots with their dorsal root ganglia
3. The filum terminale which is the continuation of piameter
4. Epidural plexus of veins formed by the lower end of vertebral veins.

5. Loose alveolar and fatty tissue, more dense in males than in females. In infants, fat is gelatinous spongy and few connective tissues facilitates a uniform and rapid spread of local analgesic solutions.

Sacral Hiatus [8]:

This is the triangular opening, in the posterior wall resulting from failure of fusion of the laminae of the 5th sacral vertebra. It's apex is at the level of the spine of 4th sacral vertebra. In some cases the apex is the 3rd sacral spine and occasionally the whole of the bony posterior wall is deficient.

When the laminae of the 5th sacral vertebra are present, the hiatus may be very small with a diameter of as narrow as 2 mm.

The hiatus is covered by sacrococcygeal membrane and pierced by the coccygeal nerves & 5th sacral nerve. The posterior sacro coccygeal membrane may be ossified in elderly subjects and making the introduction of the caudal needle almost impossible.

The distance between the sacral hiatus and dural sac may be as short as 10 mm in a neonate. Trotter showed in 53 adults that the distance between the sacral hiatus and duramater varies from 16 to 75 mm. In the presence of certain sacral malformations, this

distance might be less, and the dural sac can project even up to the level of sacral hiatus.

After age of 6-7 years, epidural fat gets more dense and is surrounded by fibrous strands, thus reducing the uniform spread of the local analgesic solutions.

The important characteristic of the caudal epidural space is that it communicates freely with the perineural spaces surrounding the spinal nerves of the Lumbosacral trunk. This has several implications. Local analgesic solutions injected into the caudal space diffuse widely into the perineural spaces, thereby improving the quality of the neural block even when dilute local analgesic solutions are used. Such a leakage into the perineural spaces also leads to an increase in the required volume of local anaesthetic. Spaces are open in children and explains why larger volume are required in children as compared to adults.

The sacrum is cartilaginous is neonates and infants, and its ossification is completed between 25 & 30 years of age. In the neonate, the long axis of the sacrum forms an acute angle with the long axis of the coccyx, thereby making it relatively easy to palpate the sacral cornua and hiatus. As age increases , the sacrococcygeal

angle increases. Thus closing the sacral hiatus and making a caudal anaesthetic technique difficult after age of 7 years.

When local analgesic solution is injected into the sacral canal, it ascends upwards in the sacral epidural space for a distance proportional to the volume of solution , force of injection, amount of leakage through the eight sacral foraminae and the consistency of the connective tissue in the space.

CAUDAL ANAESTHESIA

Selection of Equipment[8] :

Reliability of the technique and the incidence of complications largely depend on the characteristics of the needle used.

The four important characteristics of the needle

- Bevel
- Internal and external diameter
- Its length
- Presence of stylet

Sharp bevelled Needle :

Advantage : Traverse easily through the tissues

Disadvantage :

1. Characteristic "giveway" felt when sacrococcygeal membrane is punctured, may not be clearly felt with sharp needles.
2. Sharp needles have long bevel advanced further into the epidural space so that it lies entirely within it.

3. Cartilaginous sacrum can be easily traversed by a sharp and long beveled needle lead to rectal puncture or iliac vessel puncture.

Straight tipped needle with a bevel of 45 – 60 degree is ideal .

Diameter [8]:

Small needles may bend & break during procedure

Thin needles may "Giveway". It can puncture cartilaginous structures giving rise to inadverant intraosseous injection which produce effect similar to I.V. Injection. It can enter pelvic viscera and damage. It may not see the reflex of blood and cerebrospinal fluid if the needle is very small

21 to 23 G is ideal because it is rigid and large enough to allow reflux of blood or cerebrospinal fluid.

Length [8]:

Proximity of dural sac makes it dangerous to use very long needles.

Distance from the skin to the epidural space is almost always less than 20mm, even in adults. So it is not advisable to use a needle longer than 30 mm.

Needle with stylet if used prevents formation of a epidermoid tumour due to skin tag.

Epidural needle with 20 to 22 gauge are employed when one intends to use an epidural catheter via caudal route to achieve anaesthesia at higher level after radiographic conformation.

Methods for determination of the volume of Local analgesic :

Intensity of block achieved by type / concentration of local analgesic

Height of block – Depends on volume injected

Formula based on weight / age :

Armitage[8] - Practically easy to apply

High sacral - 0.5 ml / kg

High lumbar - 1 ml/kg

Thoracic level - 1.25 ml / kg

Sclhute – Steinberg formula[32] **(up to 8-12 years)**

0.1 ml / segment / yr

< 7 years – weight best predictor

Volume required in ml =

0.65 x number of segments to be blocked x body weight (kg)

To calculate the total volume to be injected.

Spiegal Formula[32] :

Total volume of injection (ml) = 4 + (D-15) / 2

Where D is the distance sepearating the sacral hiatus from the spinous process of 7th cervical vertebra.

Modified spiegal formula :

Volume of injection (ml) = 4 + (D-13) / 2

Despite larger volumes of local anaesthetic used in children as compared to adults, peak plasma levels of the local anaesthetics in children remain far below the toxic levels in adults.

As child grows, space become less compliant large volume can cause high spread of solution and an increase in the CSF concentration.

normal volume recommended for injection is 20 ml.

Objective :

To enter the epidural space at a level not only well below the spinal cord, but also below the dural sac where the sacral canal is free even of spinal nerve roots.

Patient position[21] :

Lateral decubitus position or

Prone position with pillow's underneath the hip and foot inverted to relax gluteal muscles used to perform caudal technique.

Anatomical landmarks[21] :

Classically hiatus is described as the inferior apex of an equilateral triangle formed by joining the two posterior superior iliac spine and the tip of coccyx.

Intergluteal fold is not an ideal landmark because it will not always correspond to the midline.

Left forefinger placed in coccyx tip, hiatus corresponds to the second crease of finger

Palpation of this membrane gives a characteristic feel of a membrane under tension similar to that of a fontanelle, the point of puncture is at the midpoint of this triangular space.

Technique :

Prepare area with antiseptic solution

Sterile drapes are placed around the site

Puncture the skin with the needle perpendicular and bevel parallel to sacrococcygeal membrane long fibres.

Once needle crosses the sacrococcygeal membrane, with a "give" is felt after which make an angle of 20-30 degree with the skin. This is done to prevent the needle hitching against the anterior aspect of sacrum.

Advance the needle 2-3 mm not more than the line joining the posterior superior so as to ensure that the entire bevel is within the sacral canal.

Confirmation of space :

Whoosh test[8] :

Done by injecting 7 ml of air via the needle and ask another person to auscultate just proximal to injection site, produce a characteristic whoosh sound.

Swoosh test :

Auscultation at a site just proximal to hiatus, while injecting local analgesic produce Swoosh sound

This test

Sensitivity	-	91%
Specificity	-	100%
Positive predictive value	-	100%

Useful in children to avoid air injection which cause a patchy block and a rare complication of pneumocephalus if injected in large amount and venous air embolism can occur.

Test : Commonly used to identify the space

Easy injection of drug

No resistance to injection

No subcutaneous bulge

Injection of Drug :

Do a gentle aspiration and inject over a period of 60-90 sec, irrespective of the volume injected (0.023 ml – 0.033 ml / sec)

Syringe should be repeatedly aspirated during the course of injection

Monitor the patient for any change in blood pressure / heart rate.

Faster injection cause increased cephalad spread resulting in high block and Respiratory problems

Transient increase in intracranial pressure with transient loss of consciousness / headache can occur.

If accidental vascular injection fast injection will cause rapid increase in peak plasma concentration.

On the other hand, too slow an injection increase the chances of lateralization of the block or a lower level of anesthesia since the drug tends to leak through the foramina / increase the risk of needle displacement.

Indications[8] :

Ideal for lower abdominal / lower limb surgeries.

Emergency: testicular torsion, strangulated hernia repair, paraphimosis, wound debridement of pelvis / lower limbs

Elective :

Usually combined with light general anaesthesia

Repair of inguinal / umbilical hernia / hydrocele

Orchidopexy,anorectal and genito urinary surgery

Pelvic / Hip / Lower extremity surgery

Phimosis

Contraindications :

Local skin infection

Pilonidal sinus near hiatus

Major sacral malformation – Meningomyelocele

Meningitis

Spinabifida occulta – Not a contraindication

Caution :

Hydrocephalus

Convulsion disorders

Vertebral osteo synthesis

Complications :

Due to errors of needle position and puncture technique :

1. Subcutaneous injection
2. Puncturing sacral foramen – needle may enter 3 or 4^{th} foramen, block of only the sacral root in question.
3. Vascular puncuture, Incidence : 10-15% by using short beveled needle incidence can be reduced from 10% to 1-5%
4. Dural puncture

   Dawkins reported to be 2.5%

   If punctured withdraw the needle immediately 2^{nd} caudal can be attempted provided drug injected slowly under low pressure.
5. Bone marrow / rectal injection / intra osseous injection

Puncture complication more common in difficult caudal. Maximum - three attempts only should be made.

Complications due to errors of injection :

Intravascular injection

Since epidural veins are valveless, injection immediately followed by convulsions, arrythmias, hypotension, respiratory depression.

Subarachnoid space injection

Lead to total spinal

Total caudal injection

Total analgesia even along cranial nerve distribution

Rare

? Subdural injection

Hemodynamic problems:

Rare in children below 8 years in the absence of intravenous or subarachnoid injection.

Complete or partial failure of the block :

Complete failure of block

More common > 7 years old.

Success rate increases / failure rate decreases with experience, but the failure rate will never be zero even in experienced hands.

2. Laterilization occurs in 1 in 1000 cases

When caudal is performed in lateral decubitus, 50% have a level of anesthesia 2 dermatomes higher on the dependent side.

Slow injection difference may be more than 4 dermatomes

May be due to the presence of a complete plica mediana dorsalis

3) Unanesthetized dermatomes

L5, S1, - Large size

4) Inappropriate height of the anaesthetic block

Neurologic complications :

Urinary retention :

More common if narcotics given via caudal route first act of micturition may be delayed but not trouble some.

Loss of consciousness :

Due to very rapid injection of a large volume

Nerve lesions :

Rarest complication

Poor Psychological tolerance :

Due to persistent motor block, can cause apprehension / anxiety relieved by simple assurance

Vomiting

Epidural infection / meningitis

More common with caudal catheter techniques

Shivering.

APPLIED PHARMACOLOGY

Pharmacology of Bupivacaine [26]:

Bupivacaine was synthesized in Sweden by Ekenstin and his colleagues in 1957. Introduced into clinical practice by L.J. Tulivuo in 1963.

The structure of Bupivacaine is essentially the same as Mepivacaine, with a butyl group replacing the methyl group in the piperidine ring. This increases Lipid solubility and protein binding. High potency is associated with high lipid solubility.

Physico – chemical properties :

Molecular weight	:	288 (weak base)
PKa at 25^{o}c	:	8.1
Percentage of protein binding	:	95.6%
Partition co-efficient	:	27.5 (n-Haptane pH 7.4 buffer)
Approximate Anaesthetic duration	:	175 mts (5 to 18 hrs)
Site of metabolism	:	Liver
Safe Dosage	:	150 mgs or 2.5 mg/kg
Toxicity	:	4-6 times more toxic than Lignocaine

Manufactured in concentration of 0.25% and 0.5%

Autonomic blockade produced by 0.125%

Sensory blockade with very minimal motor blockage – 0.25%

Motor blockade occurs with 0.5% solution

More sensitive on sensory nerves than motor nerves and intense anaesthesia may often be obtained without any motor blockade. This is a special advantage in the treatment of pain such as post operative, post traumatic and labour pain.

Commercially available as Hydrochloride salt. Carbonated bupivacaine is also available, act intensely and wide spread. Development of tachyphylaxis is much less common than with lignocaine.

It crosses placenta and blood brain barrier.

Pharmacokinetics :

The rate of absorption from injected site depends on the vascularity at that site.

Being highly lipid soluble, it easily penetrates nerves and vessels.

Metabolism :

Bupivacaine is one among the local analgesic that undergoes the slowest metabolism. It binds mostly to alpha acid glycoprotein.

Different methods of metabolism :

Aromatic hydroxylation

N – Dealkylation

Amide hydrolysis

Conjugation

The metabolite of N-dealkylation, N-desbutyl bupivacaine, appears in urine after spinal anaesthesia. The product Pipecolyxylidine is $1/8^{th}$ as toxic as bupivacaine. Rothenstein (1983) demonstrated that the human lungs extracted local analgesic from circulation and release back into circulation .

Bupivacaine follows a biphasic distribution

Rapid distribution phase :

In this phase, drug is distributed to highly vascular regions t ½ alpha is 2.7 minutes.

Slow disappearance phase :

The drug distributes to slowly equilibrating tissues t ½beta – 28 mts.

Slow transformation occurs in the liver, 4-10% of drug is excreted unchanged in urine t ½ (delta) = 3.5 hrs.

Clearence = 0.47 l / min

Pharmacodynamics :

Cardiovascular system :

Bupivacaine decreases the cardiac output by reducing sympathetic tone, decreasing heart rate and reducing venous return. It also causes a fall in blood pressure which is seldom profound and a fall in central venous pressure.

Toxicity :

Powerful myocardial depressant and this is made worse by hypoxia, hypercarbia and pregnancy. Ventricular arrythmias including ventricular fibrillation are more common, due to inhibition of the fast sodium channels in cardiac membrane. Bupivacaine may also block the slow calcium channels and result in conduction abnormalities leading to reentrant type of arrhythmia.

R.enatiomer is more toxic than S.enatiomer. Cardiotoxic plasma concentration of bupivacaine is 8-10 ug / ml.

Bupivacaine induced cardiac depression, can be treated with bretylium 20 mg / kg intravenously.

Respiratory System :

Seldom cause respiratory problem

Gastrointestinal tract :

Increase in gastrointestinal motility. Emptying of gastric contents is hastened.

Central Nervous system :

Eyres Rc et al (1983) on the study of deaths from local analgesic induced convulsions of mice found that a convulsant dose of local analgesic is close to the lethal dose. This was most pronounced for bupivacaine and least pronounced for lignocaine. They found that a convulsion from bupivacaine is potentially 15 times more life threatening than produced by lignocaine. These toxic effects were due to uncharged bupivacaine, highly lipid soluble which caused it to bind firmly to the myocardium, there by reducing cardiac efficiency.

According to Moore et al (1979) an arterial. Plasma concentration of 5.4 μgm / ml following intra venous bolus of bupivacaine resulted in convulsions.

Safety dosage : (2.5 mg / kg or 150 mg)

The blood concentration associated with maximum effective dose (C max) - 0.7 μmg / ml

Early signs of toxicity seen with blood concentration (Ctox) – 1.6ug / ml.

Toxicity ratio = C Tox / C max = 2.3 (Tucker et al)

However recent studies indicate that higher doses of bupivacaine 3 mg / kg may be used provided direct vascular injection is carefully avoided.

Eyres RL et al found that plasma bupivacaine concentration following administration of caudal epidural analgesia using 3 mg / kg of bupivacaine 0.25% mean blood levels of 1.2 – 1.4 μgm / ml were reached, which are well within the limits of projected toxic level.

Mechanism of action :

Sodium channel blockade:

It acts on membrane sodium channels in two ways. It acts directly on the receptors within the Sodium channel, impeding the access of sodium ion to the interior of axon, thereby preventing depolarization of the axon. It also produces non specific membrane expansion.

The sequence whereby clinically used local analgesic produce inhibition of axonal conduction has been summarized by Carvino as follows

1. Clinically all local analgesic exist in solution in both charged and uncharged forms, their relative proportions depend on the pH of the solution, pH at the site of injection and pKa of each drug .Cation form is responsible for most of the nerve blocking effect.
2. The uncharged liphophilic tertiary base form diffuse more readily across neural sheaths and the axonal membrane to reach the internal aspect of the sodium channel. The base is protonated with the cytoplasm and binds as the charged cation to a specific receptor within the internal opening of

the sodium channel and thereby inhibiting sodium conductance. The loss of membrane permeability to sodium prevents membrane depolarization and propagation of action potential.

3. The clinically used local analgesics act primarily on specific receptors located at the internal opening of sodium channel

   a) Non specific absorption within the cell membrane lipids resulting in membrane expansion and channel narrowing

   b) Diffusion of the uncharged base via hydrophobic pathways through membrane lipids to reach the specific receptor site, where protonation and binding occur within the internal opening of the sodium channel.

PHARMACOLOGY OF NEOSTIGMINE[26]

Neostigmine act as an anti cholinesterase

Acetyl cholinesterase :

It is a type B Carboxylase enzyme

At the neuro muscular junction, it occurs in the asymmetric or A12 form, which consists of three tetramers like tail.

It is a powerful catalytic enzyme catalyze 4000 molecules of acetylcholine per active site per second. Nearly half of the released acetylcholine is hydrolyzed across the synaptic cleft before reaching nicotinic acetylcholine receptors

The active surface of acetyl cholinesterase is best viewed as having two sites.

1. Anionic site – concerned with binding and orienting the substrate molecule
2. Esteratic site – where hydrolysis occurs
3. Also a second anion or peripheral anionic site proposed.

Mechanism of action :

Enzyme inhibition

Presynaptic effects

Direct effects on the neuromuscular junction

Enzyme inhibition :

Neostigmine acts by inhibiting true cholinesterase which is normally responsible for the rapid hydrolysis of the neurotransmitter acetylcholine to choline and acetic acid. It is a reversible inhibition.

Single molecule of acetyl cholinesterase able to hydrolyze an estimated 300,000 molecules of acetylcholine every minute. Because of this inhibition,degradation of acetylcholine decreases, increased availability of acetylcholine at the neuromuscular, preganglionic sympathetic and parasympathetic nerve endings.

During this reaction, acetylcholinesterase is carbamylated, which forms a covalent bond at the esteric site.

Neostigmine oxydia phoretic (acid transferring)inhibitors of acetyl cholinesterase

In addition neostigmine may also increase the presynaptic release of acetylcholine, blocks the neural potassium channels and have a direct agonistic effect.

It is possible that an excess of acetylcholine produced by acetylcholinesterase inhibition at the neuro muscular junction cause desensitization (end plate no longer responsive to acetylcholine)

Pharmaco kinetics : Dose

Neostigmine - 40 μg/ kg

Volume of distribution- 0.7 l / kg

Elimination half time - 77 min

Clearance (ml/kg/min)- 9.2

Renal contribution to total clearance (%) - 54

Speed of onset - Intermediate

Duration - 54 min

Onset of action - 7-11 min

Quarternary compound :

Poorly lipid soluble hence do not easily penetrate cell membrane barriers such as gastro intestinal tract or blood brain barrier.

Metabolism :

In the absence of renal function

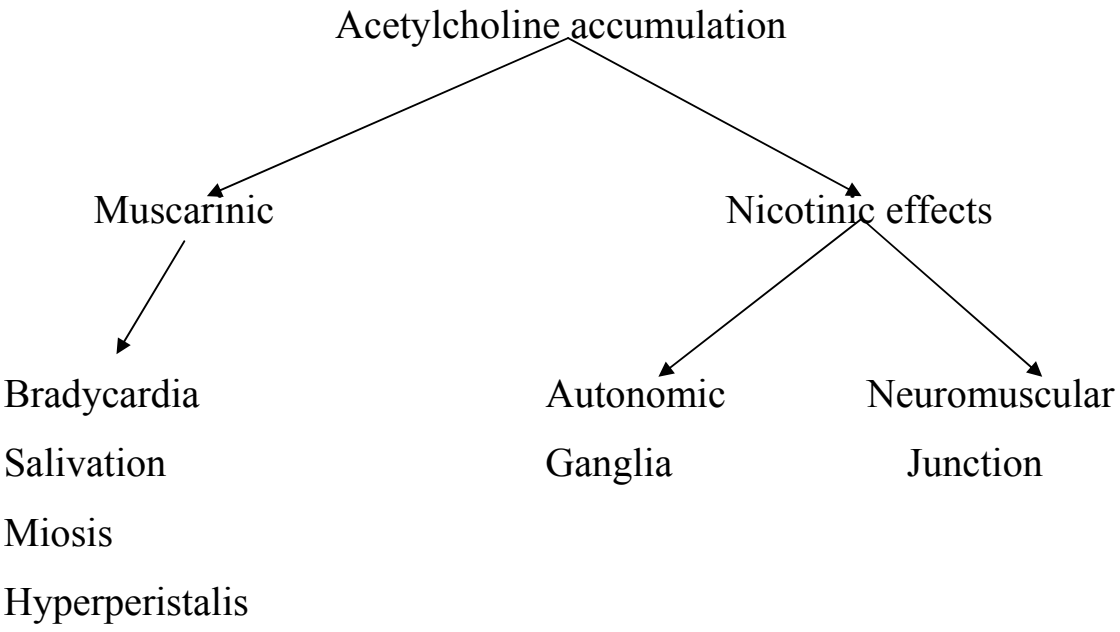
Hepatic metabolism accounts for 50% of metabolism

Principal metabolite

3 – hydroxyl phenyl trimethyl ammonium

($1/10^{th}$ the antagonistic activity)

PHARMACOLOGIC EFFECTS



Cardiovascular Effects :

Due to acetylcholinic accumulation at heart, blood vessels, autonomic ganglia, post ganglionic cholinergic nerve endings, brady cardia / brady dysrhythmias such as nodal and ventricular escape beats / asystole may occur due to slowing of conduction of cardiac impulses through the atrioventricular node. This effect due to muscarinic action inhibited by anticholinergics (preferred is Glycopyrrolate)

Gastrointestinal / Genito urinary tract :

It increases secretion and motility

Reported to cause bowel anastomotic leakage when neostigmine was used to reverse neuromuscular blockade.

Decrease gastric cardiac sphincter pressure may increase the incidence of post operative Nausea / vomiting.

Salivary Glands:

Augments production of secretion that are innervated by post ganglionic cholinergic fibres.

Bronchoconstriction due to cholinergic stimulation

Eye :

Constriction of sphincter of the Iris – miosis

Constriction of ciliary muscle manifests as disability to focus for near vision.

Increases outflow of aqueous humor & Decrease intraocular pressure.

Clinical Uses :

a) Antagonist - assisted reversal of neuro muscular blockade produced by non depolarizing neuro muscular blocking drugs upto a maximum of 70 μg / kg can be given.

b) Treatment of the central nervous system effects produced by certain drugs like atropine, inhalational agents, opioid induced respiratory depression, increase the state of consciousness in patients sedated by diazepam – Pysostigmine is more effective for above condition since it crosses the blood brain barrier.

c) Treatment of myasthenia gravis

d) Treatment of Glaucoma

e) Post operative analgesia

Intrathecal or epidural injection of neostigmine inhibits the metabolism of acetylcholine released from the spinal cord. Acetylcholine is one of more than 25 neuro transmitters that participate in spinal cord modulation of pain processing. In this regard neuraxial neostigmine produces post operative analgesia without introducing ventilatory depression characteristic of neuraxial opioids, although nausea is common[16]. Neuro toxicity does not accompany intrathecal injection of commercially available Neostigmine preparations containing paraben preservatives (Eisenach et al 1997).

d) Used for treating post operative shivering

Adverse drug Reaction :

Acute overdose (Intoxication) manifest as

Muscarinic	Nicotinic Effects
Miosis	Skeletal muscle weakness
Difficulty in focusing	Apnoea
Salivation	
Broncho constriction	Confusion
Bradycardia	Ataxia
Abdominal Cramps / loss of	Seizures
Bladder and rectal control	Coma
	Depression of ventilation

PAIN ASSESSMENT

Pain is a personal and subjective experience influenced by culture, learning, attention and psycho social variables.

As in adults there are no physiological or laboratory methods for measuring pain intensity in children. As there are developmental, cognitive and emotional differences between adults and children, Pain assessment is even more difficult to assess in children.

Measurement and assessment are used interchangeably to quantify. Measurement is the term most often used in a research context, while assessment is the preferred term in clinical context. In assessment the health provider gather's data in order to shed light on the patients experience or problem. Measurement of pain on the other hand, refers to the quantification of various aspects of the experience.

Methods[20,27,14]

Self report

Behavioural

Physiological

Self report	Behavioural	Physiological
Infant Toddler	Cry characteristics Facial expression Visual tracking Body movements Response time to stimulus Behavioural state	Heart rate Blood pressure Respiratory rate Diaphoresis
Pre schooler	Facial drawings Oucher scale Pokerchip tool Ladder scale Color scale Paediatric pain Questionnaire	Children's hospital of Eastern Ontario pain scale Procedure behaviour check list observation scale of behavioural distress, Gauvain – piquard et al scale.
School age / Adolescent	Visual analogue scales Numerical rating scales Word scales Paediatric pain questionnaire	Objective pain scale Procedure behaviour rating scale Procedure behaviour check list

Commonly used methods to assess pain in school aged children are

1. 6 point (0-5), numerical verbal pain score
2. 0 to 100 numerical scale
3. Visual analogue scale
4. Modified Mc Gill pain questionnaire

Hannallah and associates have assessed childrens post operative pain relief as Good, fair and poor depending upon the clinical observation of the status of the children.

1. Good : Cheerful, calm and cooperative
2. Fair : Miserable, restless and moderately depressed
3. Poor : Tearful, distressed and out of control

CHEOPS SCALE[27] :

A behavioural scale to measure post operative pain in children. Pain discomfort scale is one in which the observer notes certain aspects of childs behaviour and a numerical rating is applied to each. These scores are added and total score estimates the pain intensity. In this study post operative pain in children between 3-12 years old after lower abdominal / lowerlimb surgeries has been assessed using this pain discomfort scale.

Scale : Pain Discomfort Scale :

Observations	Criteria	Points
Blood pressure	+ 10% before operation	0
	+ 20% before operation	1
	+ 30% before operation	2
Crying	Not crying	0
	Crying but responds to tender loving care (TLC)	1
	Crying and no response to TLC	2
Movements	None	0
	Restless	1
	Thrashing	2
Agitation	Patient asleep or calm	0
	Mildly agitated	1
	Hysterical	2
Posture	No special posture	0
	Flexing legs / thighs	1
	Holding scrotum / Groin	2
Verbalisation of pain	Asleep or states no pain	0
	Cannot localize pain	1
	Can localize pain	2

REVIEW OF LITERATURE

1. Andrew, R. Wolf, Robert D. Valley et al in 1987. Sought to determine the optimal effective concentration (effective analgesia, minimal motor blockade and few side effects) of bupivacaine for caudal analgesia in infants and children.Three different concentration of bupivacaine 0.25% / 0.125% / or 0.06257 % used for three different groups. The volume of local anaesthetic solution administered to each child was 0.75 ml / kg. They found that bupivacaine 0.0625% was ineffective for caudal analgesia. However bupivacaine 0.125% with 1 in 200,000 epinephrine provided equipotent analgesia and significantly less motor blockade than 0.25% bupivacaine for caudal block in infants and children after superficial lower abdominal or genital surgery.

2. L.M. Broadman MD, R.S. Hannallah MD et al in 1987, Anaesth. Analg 1987 : 66 S1 – S191 a11 conducted this study to compare three different bupivacaine concentration for postoperative pain relief in three groups. The dose of bupivacaine was calculated to provide 12 segments analgesia by using a volume of 0.056 mg / kg x 12 segments as described by Takasaki. caudal block using

bupivacaine in concentrations of 0.25%, 0.30% or 0.375% respectively given . Epinephrine 1 in 200,000 was added to all solutions. It is concluded that caudal block performed with 0.25% bupivacaine containing epinephrine 1 in 200,000 produce effective post operative analgesia in children undergoing either inguinal or penile procedures Bupivacaine solutions 0.30% and 0.375 % concentration did not appear to offer any advantage when performing caudal blocks in these patients.

3. Turan, Alpurslan M.D Memis Dilek MD,

Basaran umit MD, Beyhan MD, published this study in Journal of American Society of Anaesthesiology March 2003, 98 : 3

Caudal Ropivacaine and ropivacaine(+)Neostigmine in paediatric surgery

Concluded that adding neostigmine prolonged the duration and reduced the pain scores with minimal side effects

4. Lokesh. B. Ninegegowda MD, P.K. Batra, MD, MNAMS, Virendra K. Arya MD, Pramilachari, MD, DA, MAMS. Postgraduate institute of medical education chandigarh, India.

A dose response study for caudal neostigmine used for post operative analgesia in children.compared six doses of caudal neostigmine

Six groups received neostigmine 10, 20, 30,40, 50 μg / kg one control .

Results :concluded that 30 mic/kg dose of neostigmine increased the duration of post operative analgesia and doses above 40 mic/kg increased vomiting .No episodes of respiratory depression, bradycardia, motor weakness.

5. Mohamed Abdulatif MD and Mohga El. Sanabary MSc MD, Dept. of Anaesthesiology cairo University, Egypt. @ Anaesthesia Analgesia 2002, 95 : 1215 – 1218

Studied the effect of Caudal neostigmine, Bupivacaine and their combination for post operative pain management in paediatric surgery In this study 60 patients randomly allocated to 3 groups to receive GA + caudal, Each group (n=20), 1st group received GA + caudal 0.25% bupivacaine 1 ml / kg, Second group received GA + caudal (Bupivacaine 0.25% 1 ml/ kg + Neostigmine 2 μg / kg). Third group received GA + caudal neostigmine 2μg / kg

Results :

Caudal bupivacaine + neostigmine resulted in superior analgesia compared with the other two groups. Recovery to first analgesic times were 22.8 + 2.9 hrs, 8.1 + 5.9 hr, 5.2 + 2.1hr respectively / hr neostigmine + Bupivacaine, bupivacaine, Neostigmine group.

6. Rajesh Mohayan MD, Vinod K. Grover MD, MNAMS and Pramilachars MD FAMS, Dept of Anaesthesia and intensive care. Pramilachari MD FAMS, Dept. of Anaesthesia and intensive care, PG Institute of Medical educational research Chandigarh, India.

Canadian Journal of Anaesthesia 51, 2004, 702-706, caudal neostigmine with bupivacaine produce a dose dependent analgesic effect in children.

Evaluated efficacy and duration of varying dose of caudal neostigmine with plain bupivacaine and its side effects in children undergoing genito urinary surgeries.

Conclusions :

Caudal neostigmine (2,3,4 μg / kg) with bupivacaine produces a dose independent analgesic effect (16 + 7hrs) as compared to

caudal bupivacaine (5 hrs) decrease in post op rescue analgesic consumption without adverse effects.

Incidence of Nausea and vomiting comparable in all groups. No alteration in vital signs significantly or other adverse effects.

7. Caudal epidural for post operative analgesia in male children

Jan Muhammad sheikh, Sikkandar Ali Mughal,

Sher Muhammed Shaikh, Faisal Ghani Siddiqur & Amna Memon (JLUMHS September – December 2000)

Aim :

To assess the single dose of caudal epidural with bupivacaine for post operative analgesia in children (0.25%) Bupivacaine 0.75 ml / kg)

Results :

Mean duration of analgesia 43 + 3.4 hrs, hemodynamic and respiratory parameters remained stable during the observation period. Frequency of PONV was 7% while urinary retention occurred in 1.4% patients.

8. Scope of caudal neostigmine with bupivacaine for post operative analgesia in children. Comparison with Bupivacaine.

Dr. Rudra A. Dr. Pan A.K. Dr. Acharya A, Dr. Ahmed A, Dr. Ghosh M.K.

Published in Indian Journal of anaesthesia, June 2005, Caudal administration of bupivacaine with the addition of neostigmine resulted in superior analgesia compared with caudal bupivacaine group. Requirement of initial (first) analgesic was delayed in . Caudal neostigmine + bupivacaine group. Vomiting in both groups were not statistically different.

9. Naguib. M, M.Y. Sharif, M.E.L, Gammal and A.A. Dawalatly in 1991 compared caudal bupivacaine with caudal ketamine for post operative pain relief in paediatric patients under going inguinal herniotomy. Fifty children undergoing inguinal herniotomy were allocated randomly to three groups to receive a caudal injection of either 0.25% bupivacaine 1 ml / kg with or without ketamine 0.5 mg / kg or ketamine 0.5 mg / kgwith normal saline 1 ml / kg. There was no significant difference in quality of pain relief. Post operative behaviour or analgesic requirements between the ketamine group and other two groups. The bupivacaine + ketamine mixture provided better analgesia than bupivacaine solution alone without respiratory depression or other side effects.

10. Caudal additives for post operative pain management in children. S (+) Ketamine and neostigmine N.Almenrader MD, M.Passariello MD, G. Damico MD, R. Haiberger MD, and P.Pretropaoli MD, Dept. of Anaesthesia and Intensive care medicine University of Rome, La Sapienza, Rome, Italy, Journal of Paediatric Anaesthesia volume 15 issue 2 page 143-147, February 2005.

Result : No statistical difference in duration of analgesia and sedatuib was found. Mean duration of post operative analgesia was 18+ 9.4 hrs in ketamine group and 21.8+6.7 hrs in group with neostigmine and icetamine combination. There was significantly higher incidence of Post operative vomiting after administration of caudal ketamine with neostigmine.

11) Ashitou M, Disma N, Arena C. Policlinilo Universetario, Department of Anaesthesia, Catnia Italy, published in Eur. J. Anaestheesiology 2003, Oct, 20(10), 826-30.

Levobupivacaine 0.25% compared with ropivacaine 0.25% by the caudal route in children.

Levobupivacaine provides caudal block of comparable onset and duration as provided by the same volume and concentration of ropivacaine.

12. Ansermino M, Basu R, Vandebeek C, Montogmery C, Dept. of Anaesthesia, British columbia's children's Hospital, Canada.

Nonopioid additives to Local anaesthetics for caudal block in children. Published in Journal of Paediatric Anaesthesia 2003, Sep 13(7) 561-73.

Results : Addition of clonidine to local anaesthetics solution produces an increase in duration of analgesia following caudal block in children sideeffects include sedation and potential for neonatal respiratory depression.

13. Caudal anaesthesia using two different volumes / conc. Of Ropivaccaine, (0.375% at 0.5ml / kg Vs 0.1% at 1.8 ml / kg), Silvani P, Camporesi A, Aquostcno MR, Salvo I Dept. of Anaesthesia and intensive care, V. Buzz children hospital, Italy.

Published in Minerva Anaesthesiology 2006, June 72(6) : 453-9.

Results : In children's undergoing hypospadia repair, caudal block with a high volume low concentration regimen produces prolonged analgesia and less motor block compared to low volume high concentration regimen.

14. Randomized, double blind Phase III, controlled trial comparing Levobupivacaine 0.25%, ropivacaine 0.25% and bupivacaine 0.25% by the caudal route in children. Locatelli B, Ingelmo P, Sonzogni V, Zanella A, Gatti V, Spotti A, Dimarco S, Fumagalli R. Italy. Published in Br.J. Anaesth 2005 March 94 (3) 366-71.

Results of this study was during subumbilical surgeries caudal levobupivacaine, ropivacaine and bupivacaine provided comparable analgesic efficacy. Bupivacaine produced higher incidence of residual motor blockade and longer analgesic block than ropivacaine and levobupivacaine.

15. Levobupivacaine caudal anaesthesia in children, a randomized double blind comparison with bupivacaine.

Frawley GP, Downie S, Huang GH Royal children's Hospital, Melbourne Australia, Published in Paediatric Anaesthesia 2006 July 1617) 754-60.

Results of this study showed levobupivacaine is an effective agent for caudal anaesthesia in children. . It appears to be of equivalent potency to racemic bupivacaine in children requiring lower abdominal surgery.

16. Almeida RA, Lauretti GR, Mattos AL, in Anaesthesiology 2003 Feb, 98(2) 495-8. studied the Antinociceptive effect of low dose intrathecal neostigmine combined with intrathecal morphine following gynecologic surgery. Results showed that the addition of 1-5 microgram spinal neostigmine to 100 ug morphine doubled the duration to first rescue analgesics in population studied and decreased the analgesic consumption in 24 hrs without increasing the incidence of adverse effects data suggest that low dose spinal neostigmine may improve morphine analgesia.

MATERIALS AND METHODS

A prospective single blinded randomized study was done to compare the effect of post operative analgesia in children with one group given caudal epidural bupivacaine and other group given(Neostigmine + bupivacaine)

The clinical study was carried out in fifty patients who came for surgeries in Lower abdomen and perineum (approximately 45 min – 2hrs duration) in year 2005-2007. The age group selected for this study was 3-10 years and having weight of 7-20 kgs.

Only patients belonging to ASA I physical status were chosen to avoid the influence of the associated diseases on the observation. They were divided into two groups of 25 each.

Group I received caudal bupivacaine

Group II received caudal neostigmine with bupivacaine.

Pre – Anaesthetic evaluation :

This was done prior to surgery

1. History
2. Clinical examinations
3. Relevant investigations

   Hemoglobin estimation

Urine analysis

If required serum electrolytes, blood urea and blood sugar.

4. Informed consent
5. All the children were kept nil per oral for 4-6 hrs prior to surgery

Premedication :

For the sake of uniformity, all the patients were premedicated with Inj. Atropine 0.02 mg / kg intramuscularly 45 min prior to induction of general anaesthesia, after recording basal pulse rate, blood pressure, respiratory rate and after voiding urine.

Induction and Maintenance :

After recording pulse, blood pressure and respiratory rate, 23 G venflon was used for IV line isolyte – P solution was infused. Anaesthesia was induced with 2.5% solution of inj. Thiopentone sodium 5 mg / kg and suxamethonium 2 mg/kg through I.V. and intubated with appropriate size lubricated non cuffed endotracheal tube.

After checking the air entry on both sides General Anaesthesia was maintained with halothane 0.5 – 1% with nitrous oxide and oxygen (50 : 50%) and Inj. Atracurium in titrated doses.

Child positioned for caudal anaesthesia and caudal block was given to patient's and surgeons were allowed to proceed with surgery after 10 min of block.

Group – I :

These children received bupivacaine in the dose of 1 ml / kg for inguinal surgeries and 0.5 ml / kg for perineal surgery as 0.25% concentration (diluted with 0.9% Nacl). Total dose not exceeding 3 mg / kg.

Group – II

These children received caudal neostigmine 2 μg/kg + bupivacaine 0.25% (1 ml / kg for inguinal surgeries & 0.5 ml / kg for perineal surgeries)

Intraoperatively :

Continously monitored for

Heart rate / pulse rate

Blood pressure

Oxygen saturation

If after 20 min of block of there is increase in heart rate and blood pressure 15% above the baseline, then the caudal block considered inadequate and intraoperative narcotics supplemented and the case was not taken for study.

Intra operatively parameters were monitored every 5-10 minutes till the end of surgery.

After the surgery child reversed with Inj. Neostigmine 40 μg/kg + Atropine 20 μg/kg and extubated.

After extubation recovery was assessed using Steward Score(8)

Consciousness	
Awake	2
Responding to stimuli	1
Not responding	0
Airway	
Coughing on command or crying	2
Maintaining good airway	1
Airway requires maintenance	0
Movement	
Moving limbs purpose fully	2
No purposeful movement	1
No movement	0

A score of 6 was taken as child is fully awake

In the recovery room child was observed for 2 hrs before returning to ward.

Motor blockade was assessed by using Bromage scale as follows.

Criteria	Degree of block
Free movement of legs / feet	IV Nil (0%)
Just able to flex knees with free movement of feet	III partial (33%)
Unable to flex knees, but with free movements of feet	II – Almost complete (66%)
Unable to move legs or feet	I - complete (100%)

When the child was awake, objective pain assessment, ventilatory frequency, arterial pressure, heart rate, oxygen saturation were recorded for two hours.

In wards assessments were made at 10 mts interval for the first 1 hr, for 15 mts intervals for the next 1 hr and 3,4,5,6,8,12 hrs after recovery from anaesthesia by one nurse who is unaware of the drug given.

The observer scored pain on each occasion with reference to pain discomfort scale and described by Hanallah & cheopes.

When the score was 6 and above, it was assumed that the patient has started to feel the pain and an analgesia supplement was given. Complications like vomiting, nausea, urinary retention were noted.

If child complained of pain, paracetamol syrup 15 mg / kg was prescribed and was noted by the nursing staff who were unaware of the group allocation of the patients.

Statistical Tools

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2002) developed by Centers for Disease Control and Prevention (CDC), Atlanta for W.H.O.

Using this software, frequencies, percentage, range, mean, standard deviation, x^2 and 'p' values were calculated. A 'p' value less than 0.05 is taken to denote significant relationship.

OBSERVATION AND RESULTS

The observation was recorded for both the groups as shown in the Master chart.

Table – 1 : Group allocation

Allocation	Bupivacaine 0.25%	Neostigmine
Group – I	1 ml / kg – Inguinal surgeries 0.5ml/kg – perinealsurgeries (Diluent 0.9% Nacl)	
Group II	1 ml / kg – Inguinal surgeries 0.5 ml / kg – perineal surgeries (Diluent 0.9% Nacl)	Dose : 2 μg / kg (diluent 0.9% Nacl)

Table – II - Demographic Profile

Criteria	Group I	Group II
Age (yrs)	7.0 + 2.24	7.6+2.12
Weight (kgs)	13.28 + 3.08	13.08 + 2.45
Sex (M/F)	18/7	21/4

P value : 0.5032

P > 0.05 : Not statistically significant

Group Allocation :

Caudal bupivacaine 0.25% assigned to Group I and Caudal neostigmine with 0.25% bupivacaine assigned to group II

Table I shows the group allotment, dosage of bupivacaine and dosage of neostigmine used for caudal epidural analgesia.

Clinical Study :

Table II shows the demographic profile of the patients selected for this study.

The age of the children ranged from 3-10 yrs with the mean of 7.0 $\pm$ 2.24 hrs in Group I and with a mean of 7.6 $\pm$ 2.12 yrs in Group II.

The weight of the children with the mean of 13.28 $\pm$ 3.08 in group I and in group II the mean weight of the children 13.08$\pm$ 2.45.

The two groups were comparable for age, weight and sex.

Table III – Surgical Procedures

No.	Surgical Procedures	Group I	Group II
1.	Herniotomy	9	11
2.	Urethroplasty	3	3
3.	Circumcision	5	6
4.	Undescended testis	1	2
5.	Raw area foot / Surgery	7	3

Table IV

No.	Particulars	Group I	Group II	P value
1.	Duration of Surgery (in min)	38 $\pm$ 11.37	46.67+13.16	0.0898
2.	Duration of recovery (in min)	32.8+11.04	35.37+|12.47	>0.1

P value > 0.05 is taken as statistically insignificant

Surgical procedures:

Children aged between 3-10 years scheduled for elective surgeries of the lower abdomen and perineal regions were randomly allocated into two groups.

Table III shows the list of surgical procedures performed on the two groups.

Duration of surgery and recovery time :

There was no significant difference between two groups as duration of surgery and time taken to recover from general anaesthesia is around 30-40 min in both groups.

Intraoperative Monitoring :

Heart rate, systolic and diastolic blood pressure and oxygen saturation monitored every 5 min after the caudal block.

Group	PR	SBP
I	86.45 + 3.81	96.14 + 4.13
II	88.83 + 5.43	100.20 + 7.62
P value	0.2122	0.0971

$P > 0.05$ $p > 0.05$

$P > 0.05$ is taken as statistically insignificant.

Comparison of pre operative and post operative vital data :

Monitoring	Preoperatively	Post operatively	P value
Group I			
Pulse rate	89.64 ± 5.31	89.16 ± 7.00	P > 0.05
Systolic BP	104.80 ± 6.53	102.2 ± 7.22	P > 0.05
Respiratory rate	22.26 ± 2.28	20.8 ± 1.14	P > 0.05
Group II			
Pulse rate	92.28 ± 5.54	92.52 ± 5.01	P > 0.05
Systolic BP	105.08 ± 7.26	104.58 ± 6.93	P > 0.05
Respiratory rate	21.8 ± 3.22	20.42 ± 2.43	P > 0.05

P > 0.05 is taken as statistically insignificant

Motor Blockade :

Motor blockade was assessed by using bromage scale. The patients ability to stand unaided was assessed 2 hrs after operation. In both group I and Group II all the patients were able to stand at 2 hrs after operation. The motor blockade was grade IV according to bromage scale throughout the post operative period in both group I & II. There was no significant difference of motor blockade between the two groups I and II.

Post operative monitoring :

To study the cardio vascular stability, the pulse rate, systolic and diastolic BP and respiratory rate at the maximum time of least point score in the post operative period is compared with values of preoperative period.

PDS Score

Group I	Group II	P value
1.89 ± 0.29	1.77 ± 0.42	0.3848

$P > 0.05$ is taken as statistically insignificant

PDS	Group I	Group II
0.5 - 1.0		
1.1 – 1.5	1	3
1.6 – 2.0	17	17
2.1 – 2.5	7	5
2.6 – 3.0	-	-
3.1 – 3.5	-	-
3.6 – 4.0	-	-
4.1 – 5.0	-	-

Pain Score :

The post operative pain scoring was done with reference to pain discomfort scale of Hannallah & CHEOPES. When the score was six and above, it was assumed that the patient was started to feel the pain and further observations discontinued.

Quality of Analgesia :

In group I the minimum PDS was 1.4 and maximum PDS score was 2.5 with the mean of 1.89 ± 0.29.

In group II the minimum PDS score was 0.5 and maximum score was 2.5 with a mean of 1.77 $\pm$ 0.42.

The range of PDS and number of patient in each group is given in table.

Side Effects :

No.	Complications	Group I	Group II	p value
1.	Vomiting	1	3	p>0.05
2.	Urinary retention	1	2	p>0.05
3.	Psycho somatic disturbances	0	0	p>0.05

p>0.05 taken as statistically insignificant

Duration of Analgesia :

Post operative period	Group I	Group II
0 – 2 hrs		
3 – 4 hrs	6	
4 – 6 hrs	16	1
7 – 8 hrs		
9 – 10 hrs		4
11 – 12 hrs		1
13 – 14 hrs and above		19

Side Effects :

Complications like vomiting, urinary retention and psychosomatic disturbances were noted in both groups. The comparison of side effects between the two groups are given in table.

Duration of Analgesia :

The time elapsed between the time of caudal technique to the requirement of 1st dose of post operative analgesic drug (syp. Paracetomol) was from

Group I : 4.60 ±0.92 hrs

Group II : 13.23 ± 2.98 hrs

	Group I	Group II	P value
Duration of Analgesia	4.60 ±0.92	13.23 ± 2.98	0.0000001

$P < 0.05$ statistically significant

DISCUSSION

Pain is an unpleasant subjective sensation which can better be experienced and not fully expressed, especially in children. Pain relief is even more important in children who rely mainly on their parents or care givers for their well being. In addition children lack communicative ability.

The various methods of providing pain relief have some side effects which prohibit their use, for eg, Narcotics in children, because of their respiratory depression, the other analgesics which cannot be given for sometime after general anaesthesia due to the fear of vomiting and aspiration, the objection to the needles in the case of parenterally administered analgesics.

Important non pharmacological techniques of treating acute pain include the teaching of coping mechanism (eg) hypnosis and TENS which are not applicable in children. Neverthless, regional anaesthetic techniques significantly decrease post operative pain and systemic analgesic requirements.

Among the available regional techniques caudal epidural post operative analgesia are popular in paediatrics. In the advent of new

drugs in epidural analgesia each drug is replacing the other because of their quality of pain relief and less side effects.

This work is done to compare the pain relief after below umbilical surgery surgeries in children with caudal epidural neostigmine as an adjuvant to caudal bupivacaine.

In this study, group I children received bupivacaine in the dose of 1 ml/kg for inguinal surgery and 0.5 ml /kg for perineal surgeries as 0.25% concentration. Total dose of bupivacaine not exceeding 3 mg / ml. Group II children received bupivacaine in the same dose as above along with neostigmine 2 ug/kg.

The significant findings in the study are as follows.

The two groups are comparable with respect to sex and weight. The preoperative pulse rate, blood pressure and respiratory rate are also comparable.

Cardiovascular monitoring :

In both the groups I & II there is no significant alteration in the post operative pulse rate, systolic and diastolic blood pressure in comparison to their preoperative values. I.V. Neostigmine induced bradycardia (theoretically) are not observed in caudal neostigmine in this study.

Respiratory rate :

There is no significant alterations in respiratory rate in the post operative period in the two groups compared to their preoperative values. This findings states that epidural neostigmine has no respiratory depression effect and saturation is well maintained.

Recovery from anaesthesia :

In group I, recovery time varied from 10 min to 45 min with a mean of 32.8 + 11.04 minutes. In group II, recovery time varied from 8 min to 80 min with a mean of 35.7 + 12.47 minutes. P value is > 0.1. There is no significant difference in the recovery times from anaesthesia in both groups. Caudal epidural neostigmine does not affect recovery time in this study.

Duration of Analgesia :

In group I, the duration of analgesia varied from 3.3 hrs to greater than 6 hrs.

Mean duration of post operative analgesia with caudal bupivacaine is 4.60 $\pm$ 0.92 hrs

In group II, the duration of analgesia varied from 5.3 hrs to 16 hrs.

Mean Duration of post operative analgesia with caudal neostigmine and Bupivacaine is 13.23 $\pm$ 2.98 hrs

Longer duration of analgesia produced by bupivacaine combined with neostigmine rather than caudal bupivacaine alone is statistically significant.

Correlation of the study with the previous studies as follows.

L.M. Broadman MD., RS. Hannallah MD et al in 1987. Studied the efficacy of various concentration of caudal bupivacaine, concluded that 0.25% bupivacaine effective for post operative analgesia.

Rajesh Mohayan MD, Vinod K. Grover M.D., Pramilachari M.D., FAMS (2004) demonstrated that caudal bupivacaine when combined with neostigmine prolonged the duration of analgesia and decreases the post operative rescue analgesic requirement.

SUMMARY

This study was carried out in 50 patients for surgeries in Lower abdomen, Perineum and lower limb in the age group 3-10 years with ASA-I physical status. They were divided into two groups of 25 each. Group I received caudal bupivacaine in the dose of 0.5 ml / kg for perineal and lowerlimb surgeries and 1 ml / kg for inguinal surgeries as 0.25% solution. Group II received combination of caudal bupivacaine as above dose in combination with neostigmine 2 μg / kg.

The caudal injections were given after general anaesthesia and intubation . Intra operative narcotics are with held and maintained with inhalational anaesthetic agent(halothane 0.5% to 1%)

The study demonstrated

1. Caudal bupivacaine in combination with neostigmine produced longer post operative analgesia than caudal bupivacaine alone. The mean duration of analgesia in bupivacaine group is 4.60 + 0.92 hrs Vs caudal bupivacaine / neostigmine group with mean duration of analgesia of 13.23 $\pm$ 2.98 hrs.

2. Quality of analgesia is similar in both the groups.
3. Pain relief during surgery was adequate in both the groups.

   Both groups did not require intra operative narcotics if caudal blockade was adequate
4. The incidence of nausea and vomiting, urinary retention were not statistically significant between in both groups .
5. Cardio vascular stability was well maintained in both the groups.
6. No incidence of respiratory depression in both the groups.
7. There was no prolonged motor blockade in both groups.

CONCLUSION

Caudal Bupivacaine provides adequate post operative pain relief in children but of shorter duration which can be prolonged by adding an adjuvant neostigmine (2 μg/kg) with the added advantage of adequate and safe pain relief with minimal side effects.

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PROFORMA

Department of Anaesthesiology, Madurai Medical College, Madurai.
Kiddie – Caudal
Comparison of intraoperative and post operative analgesia
in children (3-10 yrs) with
Caudal epidural bupivacaine / caudal bupivacaine with neostigmine.

Name : Age / Sex IP No. Ward

Anaesthesgiologist : Surgeon

D.O.A. : D.O.O :

Diagnosis : Surgery :

General Condition : Lab Data :

Weight Height Urine

Pulse BP Sugar

CVS RS Hb

Hydration others

Premedication

If any Route :

Time :

Technique of anesthesia : General Anaesthesia

Time :

Induction :

Maintenance ;

Duration of surgery :

Caudal epidural :

Time :

Drug :

Dose :

Volume :

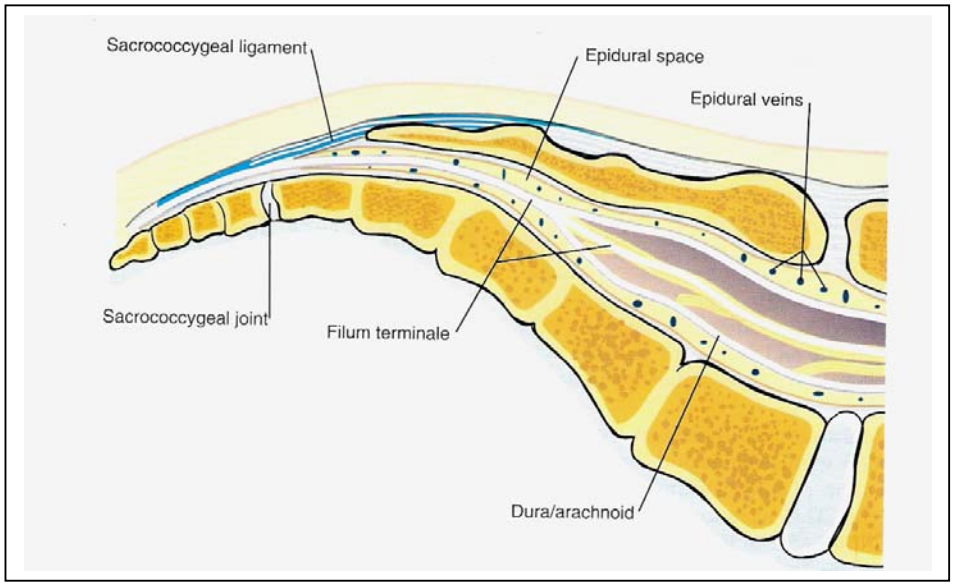
Intraoperative Observation

Time	PR	BP	SPO2	Side effects
0 hrs				
5 mts				
10 mts				
20 mts				
30 mts				
40 mts				
50 mts				
60 mts				

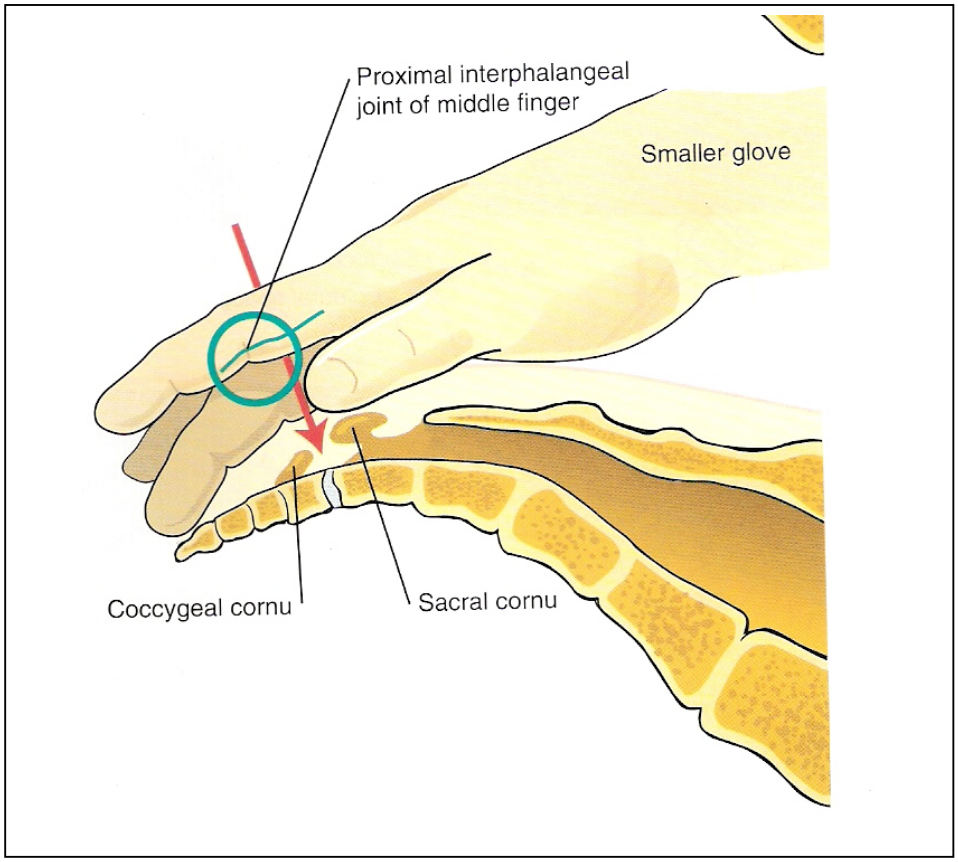
Recovery from Anaesthesia :

Steward Score

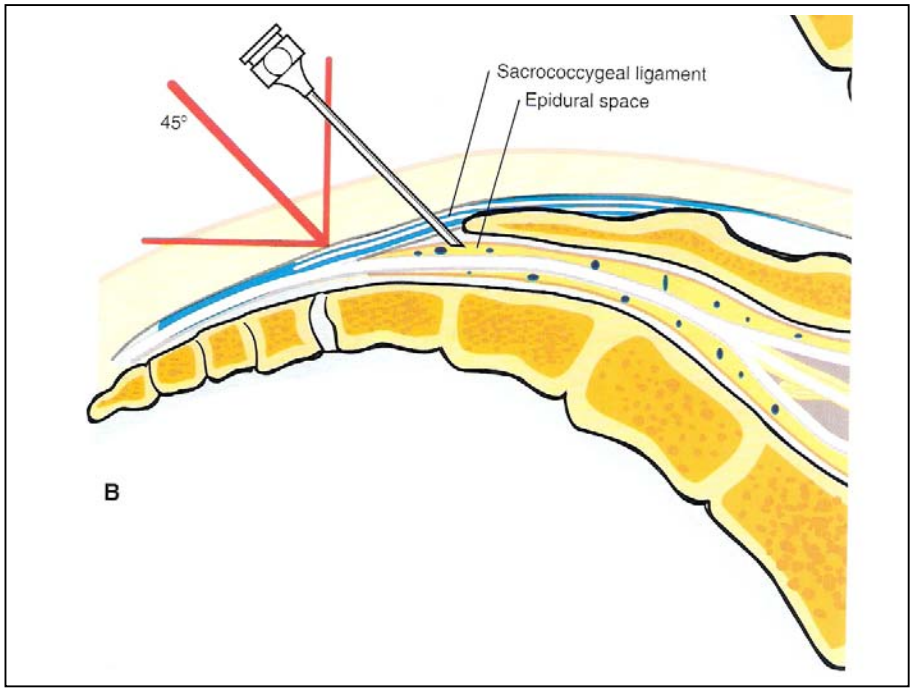
ANATOMY OF SACRAL CANAL



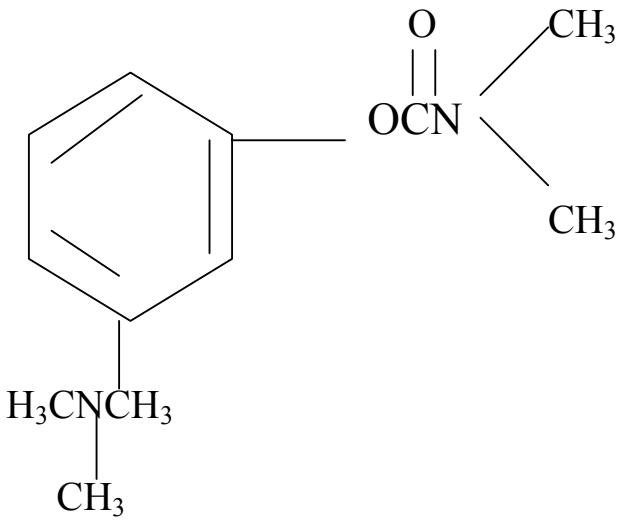
IDENTIFICATION OF SACRAL HIATUS



DIRECTION OF NEEDLE DURING CAUDAL BLOCK



NEOSTIGMINE



Post operative observations

Time	RR	BP	SPO2 RR	PDS	Bromage Scale	Side effects	Suplements of analgesia if any
0 hr							
10 mts							
20 mts							
30 mts							
40 mts							
50 mts							
1 hr							
15 mts							
30 mts							
45 mts							
2 hrs							
3-4 hrs							
4-6 hrs							
6-8 hrs							
8-10 hrs							
10-12 hrs							
12-14 hrs							

Pain discomfort scale – Hannallah & Associates (After recovery from anaesthesia)

Observation	Patients	5mts	30 mts	45 mts	1 hr	2hrs	3 hrs	6 hrs	9 hrs	12hrs	15hrs

1. Blood pressure

10% before operation 0
20% before operation 1
30% before operation 2

2. Crying

Not crying 0
Crying but responding
To TLC 1
Crying No response
To TLC 2

3. Movements

None 0
Restless 1
Thrashing 2

4. Agitation

Asleep or calm 0
Mildly agitated 1
Hysterical 2

5. Posture

No posturing 0
Flexing legs / thighs 1
Bloding groin 2

6. Verbalisation of pain

Asleep or states no pain 0
Cannot localize pain 1
Can localize pain 2

MASTER CHART - 1 STUDY GROUP

S.No.	Name	IP No.	Age	Sex	Weight	SURGERY DONE	Pulse rate	Systolic BP	Diastolic BP	Respiratory Rate	Saturation %	Pulse rate	Systolic BP	Diastolic BP	Saturation %	Pulse rate	Blood pressure	Diastolic BP	Respiratory Rate	Du.of.Analgesia(hrs)	Du.ofSurgery(mins)	Du.of Recovery(mins)	Pain discomfort score	Adverse effects
1	Vinoth	444307	5	M	12	Hypospadiasis	100	110	70	22	99	89.4	100	74	100	100	108	70	20	13	65	45	1.67	Vomiting
2	Nandhini	444354	5	F	10	Inguinal hernia herniation	90	120	70	24	97	88.4	90	60	98	98	100	70	20	15.5	35	30	2	-
3	Kamali	5099	10	F	18	Raw areafoot - SSG	108	120	70	20	98	100	110	70	99	95	90	70	20	10	40	40	1.5	-
4	Praba	55830	10	F	17	Anovestibular - transposition	90	110	70	24	97	80.2	110	70	98	90	110	70	20	10	45	30	2	Vomiting
5	Ruba sree	36487	5	F	10	Herniotomy	90	100	60	20	97	95	110	70	99	90	110	70	20	5.3	45	35	1.67	-
6	Pothiraj	50635	10	M	15	Rawarea - SSG	98	110	70	22	96	95	100	70	98	87	110	70	18	8	60	40	1.67	-
7	Stephen	56659	5	M	9	Urethral fistula repair	100	100	70	20	98	90	90	60	99	89	100	70	20	15	35	60	1.8	-
8	Santhoshkumar	OP	10	M	17	Phimosis circumcision	89	110	60	20	97	80.2	100	60	98	90	90	60	20	16	40	45	1.4	-
9	Jeyakumar	OP	5	M	12	Phimosis circumcision	100	100	70	20	98	95	122	70	99	100	100	70	20	16	65	20	2.2	-
10	Vijay	22757	10	M	16	UDT-Orchidopexy	92	100	60	20	98	94.5	108	70	99	93	122	70	18	15	75	45	1.81	-
11	Arunpandi	23248	5	M	10	Hypospadiois repair R	90	110	70	28	98	91.6	102	70	100	90	108	70	20	8.5	45	40	2.2	-
12	Murugesan	57743	10	M	12	Cong.ingu.hernia -hemio	91	100	60	24	97	88.4	102	60	100	96	102	70	18	16	50	45	2.5	-
13	Balaji	36472	5	M	12	Long inguinal hernia hem	90	100	70	20	98	84.7	96	60	100	87	102	70	16	15	65	45	2.1	-
14	Deva	OP	6	M	15	Circumcision	85	100	60	22	98	84.2	96	60	100	84	100	70	20	16	35	45	1.8	-
15	Shankar	101	5	M	17	Herniotomy	95	110	60	24	97	84.7	102	60	98	86	110	70	30	14	30	45	2.2	-
16	Kaleeswaran	OP	7	M	12	Phimosis circumcision	90	100	60	20	98	85.5	94	70	99	100	102	70	20	14	35	40	2.33	-
17	Syedibrahim	44239	10	M	11	Herniotomy	85	110	70	26	98	84.7	96	70	98	99	100	80	20	13	40	30	0.5	-
18	Karthik raja	36473	5	M	18	Cong. Hydrocele sacever	90	90	60	20	99	90.7	89	60	99	98	108	70	20	16	35	40	1.63	U R
19	Hari vignesh	36572	5	M	17	Herniotomy	85	100	70	22	95	84.2	96	60	98	89	100	70	20	10	30	30	1.75	-
20	Alagar samy	36492	8	M	15	Herniotomy	95	110	60	24	99	84.7	102	60	99	99	110	80	20	12	50	15	1.11	-
21	Kumaran	36471	9	M	8	Hydrocele sac eversion	90	100	70	24	98	80.2	90	60	100	90	110	80	22	13.5	45	15	1.67	-
22	Vijay	44754	10	M	10	Undecended testis orchi	94	110	70	20	99	95	100	70	100	90	110	70	20	15	45	45	1.43	U.R
23	Stephen	OP	4	M	11	Phimosis circumcision	90	100	70	20	100	94.5	98	60	100	92	108	70	20	13	30	25	1.67	-
24	Saravanan	OP	7	M	13	Phimosis circumcision	94	97	70	20	100	91.6	100	70	100	94	102	70	22	15	60	8	1.57	Vomiting
25	Satish	OP	5	M	15	Phimosis circumcision	90	110	60	22	99	88.4	102	60	100	87	100	70	24	16	60	45	2	-

MASTER CHART - 2 CONTROL GROUP

							PreOperative					Intra operative					Post operative								
S.No.	Name	IP No.	Age	Sex	Weight	SURGERY DONE	Pulse rate	Systolic BP	Diastolic BP	Respiratory Rate	Saturation %	Pulse rate	Systolic BP	Diastolic BP	Saturation %	Pulse rate	Blood pressure	Diastolic BP	Respiratory Rate	Du.of.Surgery (mins)	Du.of recovery(mins)	Du.of analgesia(hrs)	Pain discomfort score	Adverse effects
1	Nandakumar	op	7	M	10	circumcision	95	110	70	22	98	84.7	100	60	100	90	100	70	20	30	30	3	2.2	-
2	Surya	62352	5	M	15	hydrocele	85	100	70	24	98	82.2	96	60	99	90	110	70	22	25	40	4.3	2	-
3	Hariharan	op	10	M	18	lipoma	90	90	60	20	99	84.2	96	60	98	90	110	70	22	30	30	5	1.5	-
4	Aswin raj	58268	5	M	11	neurofibroma	85	110	70	24	99	84.7	94.6	60	99	80	100	70	24	30	15	4	1.67	-
5	Priya	36479	6	F	12	herniotomy	90	100	70	20	98	90.7	89	60	98	85	110	60	22	30	25	3.3	1.67	-
6	Jeyarubine	op	7	F	15	hamartoma	90	100	70	22	99	84.7	100	70	99	85	100	60	20	30	40	4	1.67	-
7	Kavya	59779	8	F	15	rectoplasty	85	100	60	20	98	84.2	100	60	98	85	100	70	20	40	45	5.3	1.81	-
8	Surya	62352	5	M	10	hydrocele	85	110	70	20	99	91.6	89	70	99	85	116	70	20	30	45	4.3	1.81	UR
9	Mani	op	10	M	13	circumcision	90	100	70	20	100	88.4	94	60	99	90	106	70	20	30	15	5	2.5	-
10	Kavya	op	9	F	10	FBremoval-foot	90	110	60	24	98	89.6	102	60	99	100	110	70	21	25	20	5	2.2	-
11	Palani vela	op	10	M	13	muscle biopsy	97	110	70	24	99	81.4	102	70	98	110	110	70	20	30	45	5	1.81	-
12	Sharmilini	op	10	F	13	granuloma	90	100	70	24	98	84.5	94	60	99	85	106	70	18	30	45	6	1.8	-
13	Rajkumar	43400	10	M	15	hypospadiasis	80	110	60	20	98	81.4	94	60	98	86	94	70	18	25	40	6	2	Vomiting
14	Thirumoorthy	44719	4	M	10	orchidopexy	92	100	70	18	98	90	94	70	100	90	94	70	16	30	45	5.2	1.5	-
15	Madanraj	44746	5	M	12	herniotomy	80	110	70	18	97	83	89	70	100	86	94	60	20	30	35	3	2	-
16	Manikandan	35932	6	M	10	hypospadiasis	100	110	60	16	96	90	94	70	100	99	89	60	20	60	60	4.3	1.67	-
17	Pandy	op	9	M	15	circumcision	89	100	70	20	96	89	96	60	100	85	100	60	30	25	45	5	1.67	-
18	Saran	OP	10	M	17	FB-removal foot	100	100	70	32	98	80.2	100	60	99	99	100	60	20	20	20	4	1.8	-
19	Anitha	53927	5	F	12	hamartoma	90	110	70	20	99	90	100	60	99	90	90	70	20	30	45	3.3	1.4	-
20	Siva	op	8	M	15	inguinal node	97	110	70	22	98	95	90	70	98	95	100	70	20	30	40	4	2.2	-
21	Shayam	op	8	M	11	circumcision	85	120	70	24	99	88.4	100	70	98	80	110	70	20	45	45	6	1.81	-
22	Arunpandy	50841	9	M	16	rawarea ssg	85	110	70	20	98	84.7	102	70	99	80	100	70	22	45	45	5	2.2	-
23	Munishwaren	44448	9	M	15	hypospadiasis	90	100	70	24	99	84.2	96	70	99	90	96	70	20	45	45	6	2.5	-
24	Muthu	op	10	M	14	circumcision	91	100	60	26	100	84.4	96	70	100	89	100	60	28	40	45	4	2.17	-
25	Ishwarya	44418	5	F	10	herniotomy	90	100	60	24	98	90	96	70	100	85	110	70	22	45	45	5	1.8	-

	Group I	Group II
Age	7	7.6
Weight	13.3	13.1

	Group I	Group II
Duration of Surgery	38	46.7
Duration of Recovery	32.8	35.7

	Pre Op.	Post Op.
Pulse rate	89.6	89.2
Systolic BF	104.8	102.2
Resp. Rate	22.26	20.8

	Pre Op.	Post Op.
Pulse rate	92.3	92.5
Systolic BF	105.1	104.6
Resp. Rate	21.8	20.4

GROUP I	1.89
GROUP II	1.77

GROUP I	4.6
GROUP II	13.2

	GROUP I	GROUP II
MALE	18	21
FEMALE	7	4